Progress in Influenza Vaccine Capacity Building in Vietnam

Sustainable Influenza Vaccine Production Capacity Stakeholder's Workshop
January 11, 2010

PATH
A catalyst for global health

Presentation outline

- Overview of influenza vaccine development in Vietnam
- Specific development activities
- PATH-BARDA Cooperative Agreement
- Next steps

Building influenza vaccine capacity in Vietnam

- Human vaccine development in Vietnam against pandemic influenza has been a high priority for several years in response to H5N1.
  - Strongly supported by the governments of Vietnam, the United States, Japan, the WHO, and others.
  - Three entities initially engaged in human influenza A/H5N1 vaccine development and production.
  - Surveillance system to identify prevalence and seasonality of influenza.
  - Progress towards identifying gaps and establishing steps to continue development towards licensure.

The vaccine in general

- Three established manufacturers, 1 research institute with strong interest in producing influenza vaccine
- rgH5N1 seed virus
- Whole-inactivated virus
- Alum adjuvant
- Different substrates
- All now focusing on H1N1 2009 vaccine

VABIOTECH – funding

- A Vietnam Government-Supported Grant National Project (MoST) (2005-2006)
  - Research and Development
  - Pre-Clinical studies

  A DHHS/CDC, US. Supported Grant Project (2008-2009)
  - Pilot scale production;
  - Equipment procurement;
  - Technical assistance;
  - Clinical study (Phase I and II)

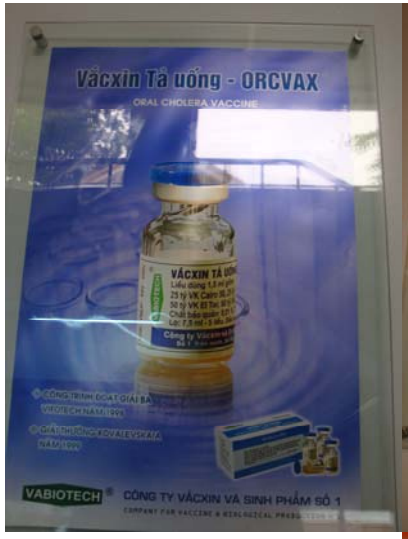
VABIOTECH®

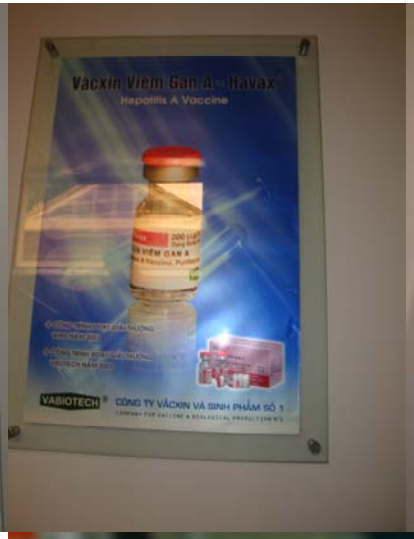
VABIOTECH – progress

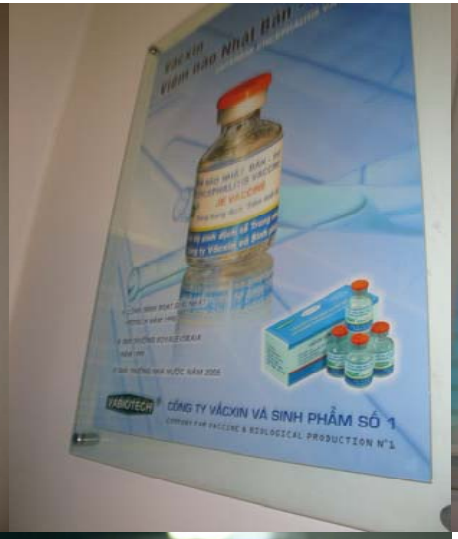
- Primary monkey kidney cell-based
- Completed the production process and manufacture of H5N1 clinical lots
- Showed immunogenicity in animals
- Conducted Phase 1 and 2 clinical studies with H5N1
  - N=30, 30ug HA+alum, 2 doses. No SAEs, only mild local pain. Seroconversion >95%, cross-clade >76%
- Focusing on H1N1 in different cell substrate, using similar process from H5N1
- Pilot capacity target: 1.2M doses/year – 100,000 doses/month
- Plans for scale up: 20M+ doses/year

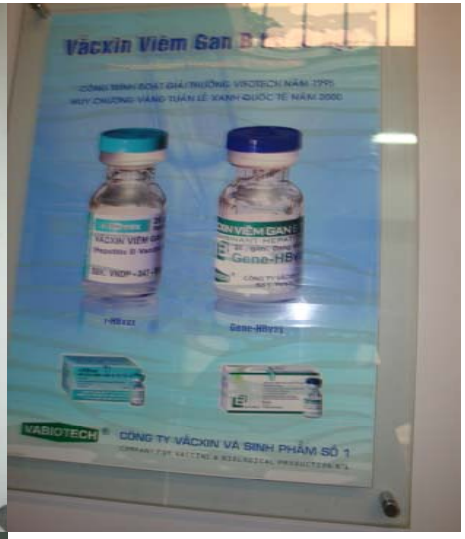
VABIOTECH ®

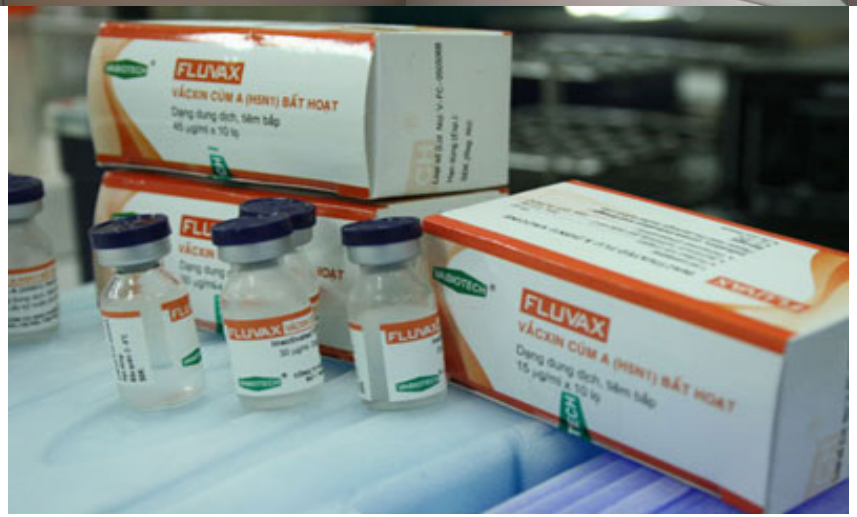
VABIOTECH – vaccine



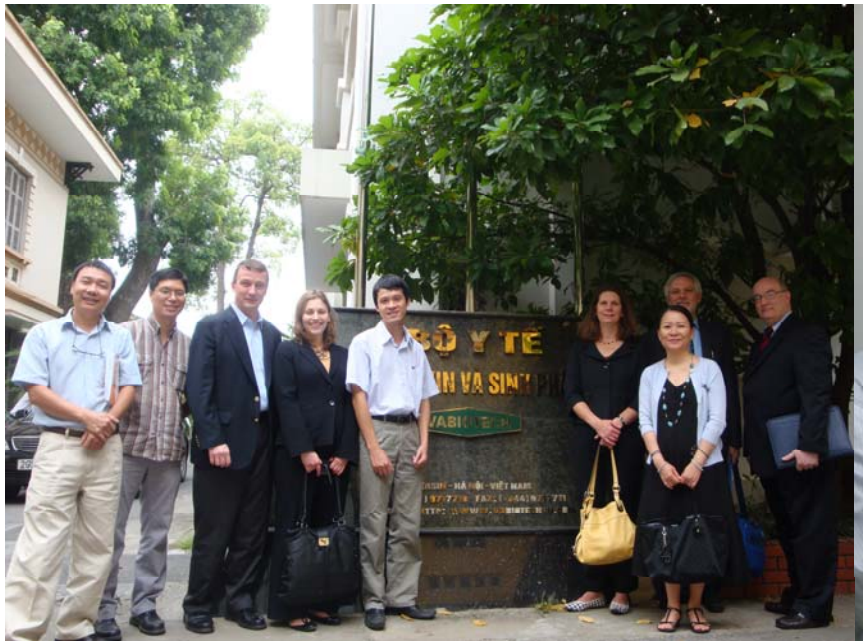








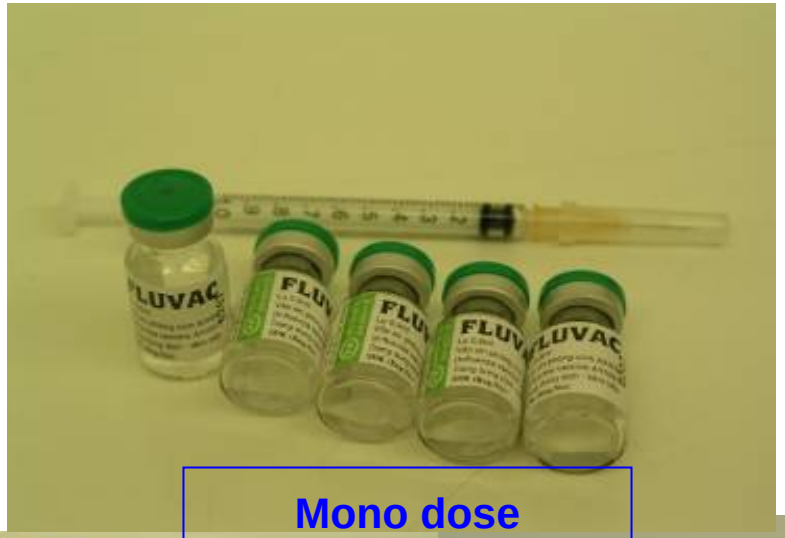
VABIOTECH – facility



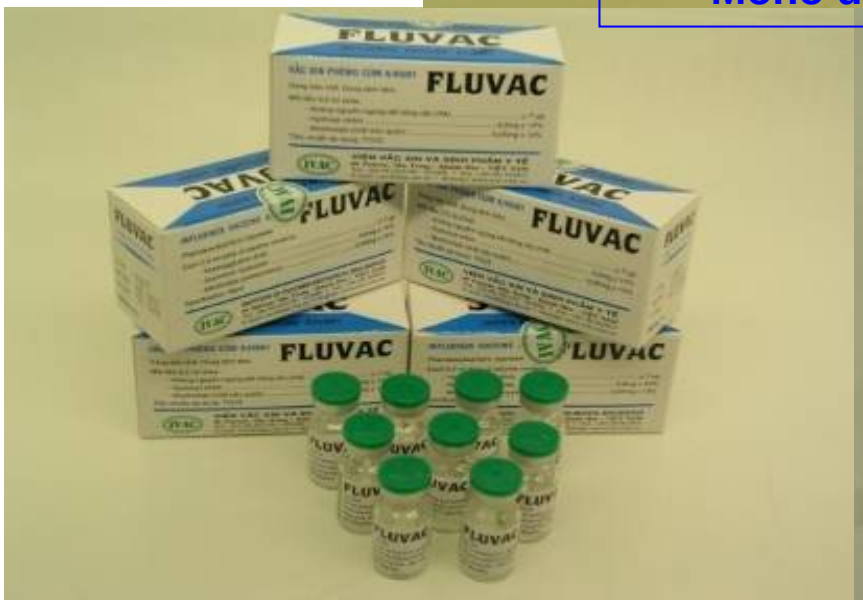
IVAC – progress

- Received financial support from Vietnam (MOH) and from the U.S. and Japan governments through the WHO
- Received technical guidance from the WHO and NVI
- Embryonated chicken egg-based
- Produced more than 5 lots of H5N1 that met WHO requirements in pilot facility
- Completed preclinical stage to show immunogenicity in animals
  - HI titers >40 in 100% mice; HI titers >320 in 77% mice, 100% GPs, 96% chickens
- Focusing on H1N1 to be produced in new facility
- Full capacity targeted to 1.5M to 3M doses/year

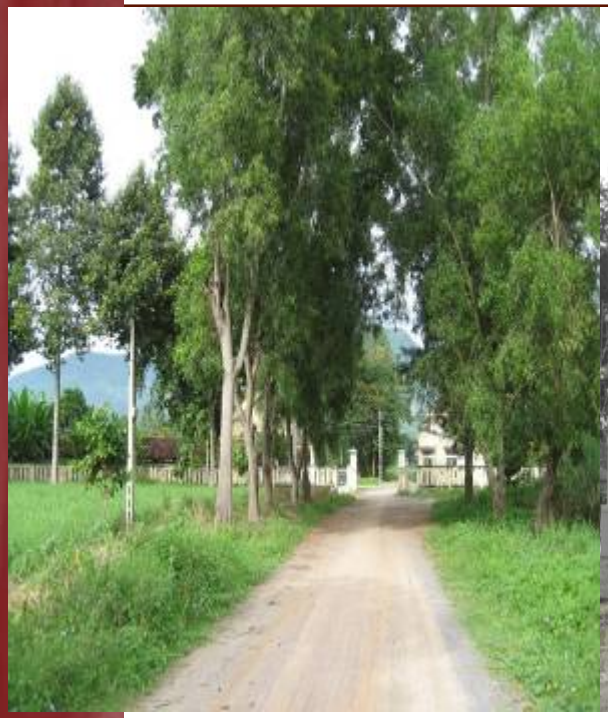
IVAC – vaccine

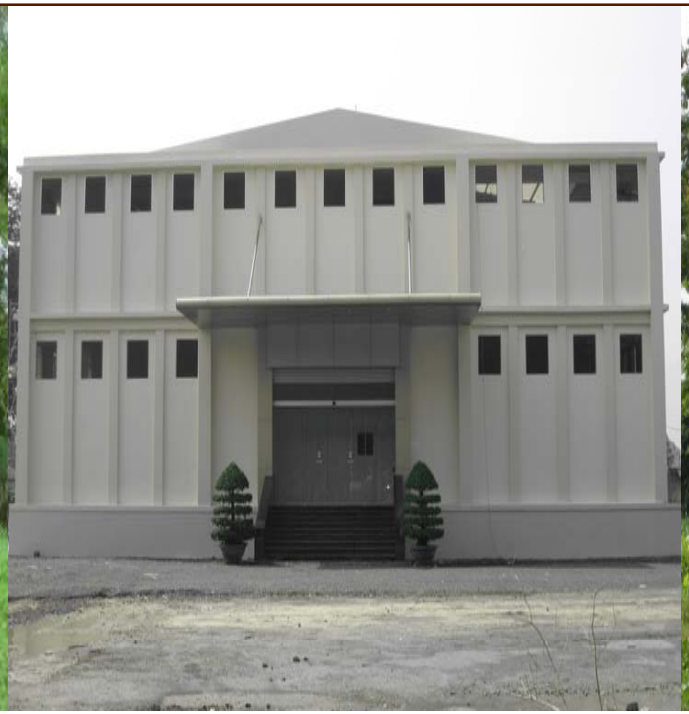


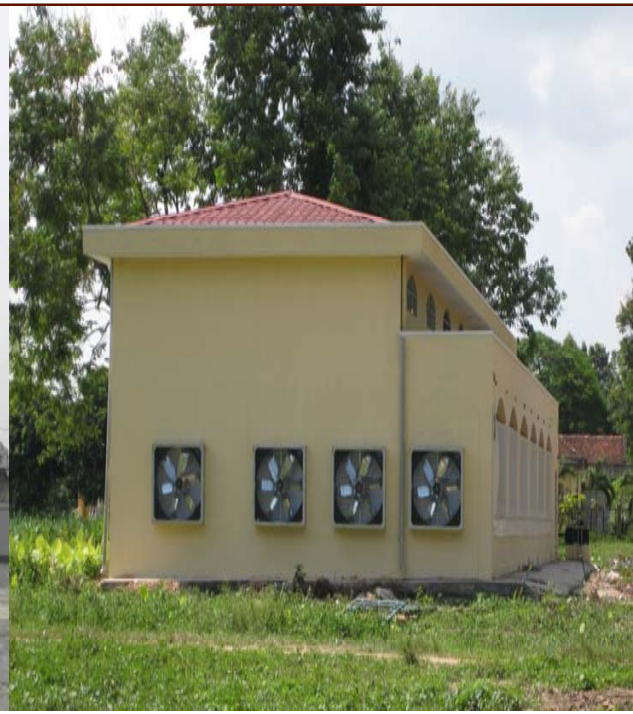
Mono dose



IVAC – new influenza facility







A factory of approx. 800 m^2 will be built including Production division, QC and offices

Chicken farm and other facilities will be nearby

- ***Capacity:*** ***500,000 doses/year with expansion capacity up to ~ 1M doses/year***
- ***Building site:*** ***Suoi Dau farm (20km far from HQ of IVAC)***

Institute Pasteur - HCMC

- Received financial support from the Vietnam government (MOH) for process development
- Vero cell-based
- Completed production process for H5N1
- Completed preclinical stage to show immunogenicity in animals (10ug doses fully protected mice)
- In the past they have manufactured BCG vaccine, they do not currently manufacturer any and long term plans for production of influenza vaccines are unclear

POLYVAC

- Established in 1994, includes 3 facilities:
  - OPV facility
  - Measles vaccine facility
  - Monkey breeding center
- Very new interest in influenza vaccine production to help address the H1N1 outbreak
- Received financial support from the Vietnam government (MoST) for process development
- Plans to explore either MDCK or Vero cell production
- While they do manufacture some vaccines, long term plans for production of influenza vaccines are unclear

Key issues and next steps

- Complete quality assessment of facilities/process to ensure cGMP compliance
- Scale up processes from pilot scale
  - Technical training and support is needed
- Submit regulatory dossier for approval to conduct clinical trials
  - Need to clarify regulatory process for clinical evaluation and licensure (Dr. Huong)
  - Need to enhance clinical infrastructure (Dr. Huong)
- A need to enhance surveillance, burden of illness, and policies for uptake and use of seasonal influenza
- Funding and technical support is critical for all companies

PATH-BARDA Cooperative Agreement

- Three-year program, $7.9M, started Oct. 2009
- Primary goal: Continue progress that has been made in advancing vaccine production in Vietnam
  - Evaluate current status of various development programs in Vietnam
  - Complete cGMP production of clinical trial material (CTM)
  - Conduct Phase 1 & 2 clinical trials with CTM produced in Vietnam
  - Identify additional activities to enhance in-country capacity for all manufacturers (workshops on regulatory guidelines/strategies, clinical pathways, vaccine usage, immunological assays)

PATH-BARDA Cooperative Agreement

- Next steps
  - U.S. and Vietnam teams in place
  - Conduct manufacturing readiness assessment
  - Conduct clinical readiness assessment
  - Identify gaps and develop workplan to manufacture CTM
  - Begin planning process for in-country workshop(s)

Summary

- Several approaches to enhance influenza vaccine capacity are in active development in Vietnam
  - Strong support from government of Vietnam (MOH, MoST)
  - Strong alliances to the United States Government and international stakeholders such as the WHO
  - Financial support from the United States Government and Japan
  - Strong alliance and technical support from the WHO
  - Strong technical training from NVI
- New PATH-BARDA cooperative agreement will build upon this success to ensure production of cGMP-quality vaccine and evaluate in the clinic
- Continued and additional support is strongly needed to continue development, broaden to seasonal influenza, and create models for sustainable vaccine production and use

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